STATINS: PRE-CONCEPTION AND CONTRACEPTIVE ADVICE FOR CHILD-BEARING AGE WOMEN AND LIPID CONTROL IN PREGNANCY

KEY RECOMMENDATIONS

- Women of child-bearing age on, or for consideration of statins, should have appropriate **pre-conception advice** and **be offered appropriate contraception**.
- Women planning to conceive should be advised to **stop statins at least 3 months before planned conception** unless an alternative management plan has been discussed in secondary care.
- Women found to be **on a statin in pregnancy** should be:
  - Advised to **stop the statin immediately**
  - Be urgently referred to a consultant-led obstetrics clinic
  - **Should be reassured that the risk of harm to the foetus is thought to be low**
- **Bile acid sequestrants are a possible alternative to statins** in pregnancy, ezetimibe and niacin are not and there may be **rare indication for the use of statins in pregnancy**; this should be established in **secondary care**.
- **Lipoprotein-apherisis is reserved for very high-risk patients** and is a tertiary service.

WHY ARE THESE YOUNG WOMEN ON A STATIN?

Usually, because they have familial hypercholesterolemia (FH) or other much rarer lipid disorders putting them a very high risk of cardiovascular disease. It is important for FH patient to have tight lipid control, especially in patients with existing CVD. In women of child bearing age, this risk must be balanced against the possible risk to the foetus in pregnancy. It is important to stress that "with early identification of FH in women and proper planning, most women with FH can have healthy pregnancies and healthy children" [1].

ARE STATINS ACTUALLY DANGEROUS TO THE FOETUS?

Early uncontrolled case series reported congenital anomalies associated with statin use [2] but, although we do not know for sure, **statins in pregnancy are probably lower-risk then initially thought**.

A European multicentre observational prospective controlled study comparing 249 exposed pregnancies statin exposure to and 249 control cases "did not detect a teratogenic effect of statins" [3] but was too statistically underpowered to warrant a change in recommendations of statin discontinuation during pregnancy. In the same period, a systematic review of human and animal studies suggested that "statins are unlikely to be teratogenic"; the evidence did not consistently point to teratogenicity and, in human cases, no pattern or common mechanism for observed foetal damage could be established [4]. A similar review of 2016 again supported the conclusion that **"statins are probably not teratogenic"** [2]. Nevertheless, **guidelines err strongly towards statin avoidance**.

WHAT SHOULD I DO IF A PREGNANT PATIENT IS FOUND TO BE ON A STATIN?

It may be appropriate for this patient to be on a statin: statins may help prolong pregnancies in pre-eclampsia [8] and are being used in clinical trials (from 20 weeks of gestation) [1] or risk/benefit analysis in secondary care may warrant the statin.

However, if there is no indication for the statin, the patient should be advised to stop the statin immediately and *offered* an urgent referral to an obstetrician, she should be **reassured that the likelihood of foetal complications is low** [1,7].

CURRENT GUIDELINES

The NICE Familial hypercholesterolaemia: identification and management Clinical guideline [CG71] advises for women of childbearing age that [5]:

- The risks for future pregnancy and the foetus while taking lipid-modifying drug therapy should be discussed. **This discussion should be revisited at least annually**.
- Lipid-modifying drug therapy should not be taken if they are planning to conceive or during pregnancy, because of the potential risk of foetal abnormality.
- Lipid-modifying drug therapy should be stopped **3 months before** they attempt to conceive.
- Women [with FH] who conceive while taking statins or other systemically absorbed lipid-modifying drug therapy should be advised to stop treatment immediately **and they should be *offered* an urgent referral to an obstetrician for a foetal assessment.** Women should be fully informed about the nature and purpose of the assessment. They should be full information to consider their options (including the advantages and disadvantages) of continuing with their pregnancy.
- COCPs are not generally contraindicated for women and girls being treated with lipid-modifying drug therapy but as they carry a small increased risk of cardiovascular events, alternatives should be considered.

A similar position is held by the US National Lipid Association Expert Panel although the statin (and other systemically absorbed lipid-regulating drugs) "washout" period is defined as "at least 4 four weeks" [6]; the washout period remains 3 months in the guidelines issued by the International Familial hypercholesterolaemia Foundation [7].

SUITABLE ALTERNATIVE TREATMENT

When women with FH stop statins, their cholesterol levels rise rapidly. One option is just accepting the additional cardiovascular risk (most women in this situation will have had years of non-statin taking for all sorts of reasons and are just adding to this risk a bit).

The recognised alternative is the use of **bile acid sequestrants** as these are not systemically absorbed [1,9]; NICE guidelines do not specifically discuss bile acid sequestrant use as a statin substitute in the intrapartum period but do consider their use more generally in patients who are "intolerant of statins" [5]. Such initiation should take place in secondary care, ideally in a joint metabolic/obstetric clinic not least because **sequestrants lower absorption of lipid-soluble vitamins**, and appropriate vitamins A, D and K and folic acid supplementation should be considered. Other possible treatment exists such as Mipomersen (an antisense inhibitor of apoprotein-B synthesis) and lipoprotein apheresis[1]. The former is not available in the UK, the later can only be done in one of a few specialist centres in the UK and is limited to very high risk patients (e.g. homozygous FH (HoFH))1,5.

As always, remember that **lifestyle modification (with a low-fat, low-cholesterol diet, regular exercise and smoking cessation) are highly advisable** and play a key role in CVD risk reduction**.**

AUDIT SUGGESTIONS

1. Audit your practice to identify women of childbearing age (typically defined as >=15 and <=45 years old) on statins or any other systemic lipid-reducing medication (e.g. ezetimibe). Review the need for a statin in this situation and offer **pre-conception** and **contraceptive advice** to any women whose risk/benefit analysis suggests benefit from continuing a statin - and who have not had this advice.

2. Audit your practice to identify pregnant women on statins or any other systemic lipid-reducing medication (e.g. ezetimibe, niacin) and, unless the medication has been deemed necessary by secondary care physicians and the patient has been appropriately counselled. Advise them to stop the systemic medication immediately. *Offer* **an urgent review** and **urgent referral to an obstetrician** but **reassure the patient the risk to the foetus is low.**

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